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GAMBEL, R. EXAMINER

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DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

This application has been examined Responsive to communication filed on _____ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. Notice of References Cited by Examiner, PTO-892.
2. Notice re Patent Drawing, PTO-948.
3. Notice of Art Cited by Applicant, PTO-1449.
4. Notice of Informal Patent Application, Form PTO-152.
5. Information on How to Effect Drawing Changes, PTO-1474.
6. _____

Part II SUMMARY OF ACTION

1. Claims 1-70 are pending in the application.

Of the above, claims _____ are withdrawn from consideration.

2. Claims _____ have been cancelled.

3. Claims _____ are allowed.

4. Claims 1-70 are rejected.

5. Claims _____ are objected to.

6. Claims _____ are subject to restriction or election requirement.

7. This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. Formal drawings are required in response to this Office action.

9. The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are acceptable. not acceptable (see explanation or Notice re Patent Drawing, PTO-948).

10. The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been approved by the examiner. disapproved by the examiner (see explanation).

11. The proposed drawing correction, filed on _____, has been approved. disapproved (see explanation).

12. Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has been received not been received been filed in parent application, serial no. _____; filed on _____.

13. Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. Other _____

EXAMINER'S ACTION

15. The disclosure is objected to because of the following informalities:

Applicant's reference to U.S. Patent No. 4,879,263 on page 11, line 11 is inappropriate since this patent is drawn to a sliding member of high strength and high abrasion resistance. Applicant should delete reference to this patent in the specification.

Applicant refers to copending applications 07/800,474 and 07/938,079 in the specification; applicant should update their status.

16. 35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

17. Claims 1-40 are rejected under 35 U.S.C. § 101 because the invention as disclosed is inoperative and therefore lacks utility. The specification fails to establish the utility of the claimed vaccines or methods as therapeutic regimens in treating human prostatic cancer.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Concerning vaccines in general, the antigenic or immunogenic nature of a protein or an anti-idiotypic antibody does not necessarily correlate with its ability to confer protective efficacy as a vaccine.

Applicant discloses that prostate cancer continues to be refractory to treatment despite many years of efforts to improve therapy. Similarly, applicant discloses that vaccine development has been slow and no vaccine approved by the FDA for marketing currently exists for any form of cancer. Applicant has not provided any evidence a priori that establishes the efficacy of the instant invention drawn to an antigen (e.g. protein, peptide or fragment thereof) overrepresented in the prostate gland (e.g. PSA, PSMA or PAP) for the treatment of human prostatic cancer.

In the instant application where the prostate gland itself is not eliminated, then a further problem could occur by the claimed methods by eliciting prostate specific immunity. The generation of an immune response against self even if it is against tissue-specific antigens could elaborate into an autoimmune response against other antigens of the host.

Therefore it does not appear that the asserted utility of the claimed methods and compositions for treating humans would be believable *prima facie* to persons of skill in the art in view of the contemporary knowledge in the art. See MPEP 608.01 (p).

18. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19. The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure and failing to present the best mode contemplated by the applicant for carrying out the invention.

A) Applicant has not disclosed how to use the claimed vaccines and methods to treat prostatic cancer as a therapeutic regimen in humans. There is insufficient evidence of the invention with respect to the *in vivo* operability of the claimed prostate-specific proteins, peptides or fragments thereof to use applicant's invention for the reasons discussed in detail in the previous rejection made under 35 U.S.C. § 101 (see paragraph 17). No examples or nexus is provided in the application of prostate-specific antigen-mediated therapy as a therapeutic regimen for human prostate cancer. Therefore it does not appear that the asserted operability of the claimed methods and compositions for inducing antitumor responses in potential or actual prostate tumor-bearing subjects would be believable *prima facie* to persons of skill in the art in view of the contemporary knowledge in the art. It appears that undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification alone.

B) Applicant discloses that the antigens overrepresented on prostate includes any other antigens substantially uniquely present on the prostate gland so that prostate derived tissue can be distinguished from other tissues by virtue of the presence of these antigens (see pages 9-10). There is no evidence relating to overrepresented prostate-specific antigens other than PSA, PSMA and PAP to practice all of the claims vaccine compositions and methods embraced by the claims. The specification has not provided sufficient direction or guidance to one of skill in the art to properly select prostate antigens other than PSA, PSMA that are required to enable the broadly claimed compositions and methods. It appears that undue experimentation would be required of one skilled in the art to practice the broadly claimed compositions and methods using the teaching of the specification alone.

20. Claims 1-40 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification (see paragraphs 18-19).

21. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 C.F.R. § 1.75(d)(1) and M.P.E.P. § 608.01(l). Correction of the following is required: It is not clear what is meant by claim 6 reference to a "neoadjuvant". The various adjuvants disclosed include liposomes, FCA, alum, etc. (see pages 14-15). The subsequent art rejections will be made on these disclosed "neoadjuvants" in the absence of any other disclosure.

22. Claims 1-40 are rejected under 35 U.S.C. § 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-40 are indefinite in the recitation of "at least one antigen overrepresented in the prostate gland", "peptide", "a fragment thereof", "portion", "portion thereof", "active ingredient", "effective portion", "portion being less than the complete antigen" and "exhibits posttranslation modification different from those of PSA produced in human cells" because their characteristics are not known. This language is vague and indefinite since it encompasses potentially thousands of different proteins or peptides and it is not apparent from the disclosure which particular proteins or peptides are being referred to. It would require undue experimentation to produce all such possible proteins and peptides without more explicit guidance from the disclosure. No direction or guidance is provided to assist one skilled in the art in the selection of all

such possible vaccine derivatives nor is there evidence provided that all such derivatives would be therapeutically effective. It appears that undue experimentation would be required of one skilled in the art to practice the claimed methods and compositions in providing effective vaccines for prostatic cancer using the teaching of the specification alone.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

23. Claims 1-40 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-40 are indefinite in the recitation of "vaccine" and "composition". Minimally, the pharmaceutically acceptable carrier should be recited in the claims as long as there is appropriate support in the specification. In addition, the specific function of the composition and the effective amount of the active ingredient can be recited. Presently, the claims as recited read on a compound per se.

B) Claims 3 and 9 are indefinite in the recitation of "PSA", "PSMA" and "PAP" because these terms should be spelled out for clarity.

C) Claim 6 is indefinite in the recitation of - "neoadjuvant" - because its metes and bounds are not known. Also, quotations have no place in the claim language since such language should be clearly defined. Finally, there appears to no antecedent basis of this term in the specification (see section 19 C above).

D) Claim 34 is indefinite in the recitation of "with the proviso that said antigen is other than human prostate specific antigen (PSA) produced in human cells" because it is unclear whether this refers to antigens other than PSA or to antigen derived from cells other than its natural host.

The amendments must be supported by the specification so as not to add any new matter.

24. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

25. Claims 1-40 are rejected under 35 U.S.C. § 103 as being unpatentable over Chu et al. (1449, # ; U.S. Patent No. 4,446,122) in view of Dai et al. (FASEB J., 1988), Deguchi et al. (Cancer Research, 1986), Brown et al. (U.S. Patent No. 5,262,177) and Alving (J. Immunol. Methods, 1991) and the art-known vaccine and recombinant technology acknowledged throughout the specification. Claims 1-40 are drawn to vaccine compositions and methods that employ prostate-specific antigens in the treatment of prostatic cancer.

From a reading of the specification, the alleged novelty of the instant application appears to rest with the statement that there has been no report of the use of antigen protein or an antiidiotypic antibody bearing the internal image of the prostate antigen as a vaccine for prostate cancer (see page 2, lines 19-23). Applicant discloses that the prostate antigens, surgical treatment associated with prostate cancer, adjuvant formulations and recombinant technology were all known at the time the invention was made; therefore the claimed limitations of these aspects were known or obvious at the time the invention was made. Similarly, Brown et al. teach the art-known recombinant viruses in the derivation of vaccines (including adjuvants) based on tumor-associated antigens. Also, Alving teach the art-known use of liposomes as carriers of antigens and adjuvants in vaccine technology.

Chu et al. teach the characterization of the PSA antigen (see entire document), its use in immune-specific chemotherapy (column 6, paragraph 1) and its use preparing diagnostic antibodies and vaccine preparation (see column 7, paragraph 3). Dai et al. teach the generation and characterization of anti-idiotypic antibodies for prostate tumors (see Abstract). Deguchi et al. teach the use of PAP-specific antibody conjugates for the treatment of prostate tumor (see entire document). Therefore the prior art did recognize the use of prostate-specific antigens in the derivation of therapeutic regimens to treat prostate cancer.

One of ordinary skill in the art at the time the invention was made would have been motivated to select and evaluate the efficacy of prostate-specific antigens as vaccines in the treatment of human prostate cancer. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention was a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

26. No claim is allowed.

27. Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CMI Fax Center telephone number is (703) 308-4227.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.


Phillip Gambel, Ph.D.
June 16, 1994


DAVID L. LACEY
SUPERVISORY PATENT EXAMINER
GROUP 180
